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L7 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:912224 CAPLUS
DOCUMENT NUMBER: 147:269196
TITLE: Methods for inhibition of lymphangiogenesis and tumor metastasis
INVENTOR(S): Varner, Judith A.; Garmy-Susini, Barbara
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 90pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007092471	A2	20070816	WO 2007-US3205	20070205

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-765068P P 20060203

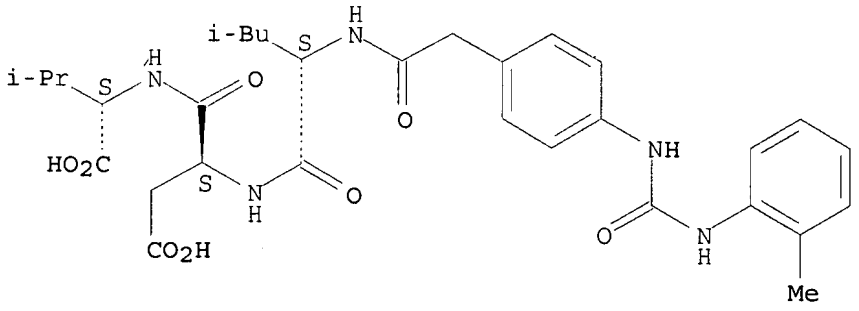
AB The present invention is directed to compns. and methods for inhibiting the development of new lymphatic vessels, and for inhibiting tumor cell dissemination through the lymphatics. In preferred embodiments, the present invention utilizes agents that inhibit the specific binding of integrin α4β1 (α4β1, VLA-4) to one or more of its ligands. The invention further relates to methods for screening test compds. for their ability to inhibit undesirable lymphangiogenesis and/or tumor metastasis.

IT 181520-66-1 181520-85-4 187735-94-0
187737-40-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of lymphangiogenesis and tumor metastasis)

RN 181520-66-1 CAPLUS
CN 1,3-Benzodioxole-5-propanoic acid, β-[[(2S)-4-methyl-1-oxo-2-[[[4-[[(phenylamino)carbonyl]amino]phenyl]acetyl]amino]pentyl]amino]-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

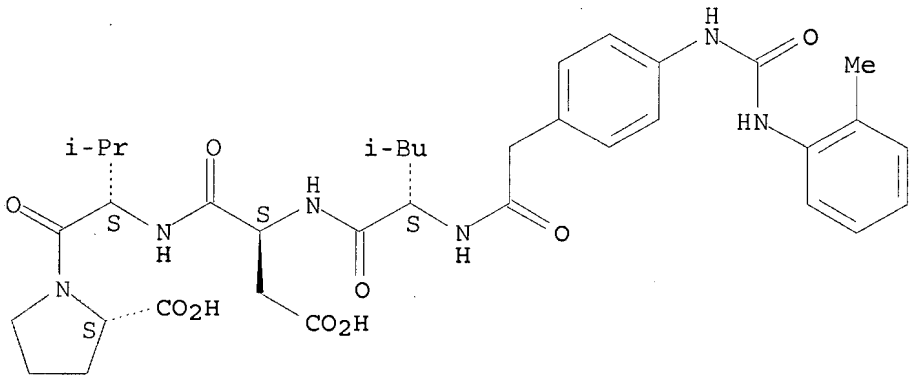


L7 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:560477 CAPLUS
TITLE: Effect of enalapril on the in vitro and in vivo peptidyl cleavage of a potent VLA-4 antagonist
AUTHOR(S): Karanam, B. V.; Jayraj, A.; Rabe, M.; Wang, Z.; Keohane, C.; Strauss, J.; Vincent, S.
CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Xenobiotica (2007), 37(5), 487-502
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal
LANGUAGE: English

AB BIO1211 is a small peptidyl potent antagonist of the activated form of α4β1 integrin. The effect of enalapril on the in vitro and in vivo cleavage of BIO1211 was investigated. In heparinized blood, plasma and rat liver, lung and intestinal homogenates, BIO1211 was converted rapidly to BIO1588 by hydrolytic cleavage of the terminal dipeptide moiety. This cleavage could be inhibited by EDTA and the ACE inhibitor, enalaprilat, the de-esterified acid derivative of enalapril. Enalaprilat inhibited the hydrolysis of BIO1211 in a concentration-dependent manner with IC50 values of 2 nM in human and sheep plasma and 10 nM in rat plasma. In rat lung homogenate supernatant, the maximum inhibition of the conversion of BIO1211 to BIO1588 was .apprx.80% at 1 μM with no further effect up to 100 μM of enalaprilat. Following a concomitant IV administration of enalapril and BIO1211 at 3 mg/kg each, the AUC and the half-life values of BIO1211 increased 18- and 10-fold, resp. The AUC of BIO1588 decreased .apprx.2-fold with no change in its plasma half-life. When rats were dosed i.v. with enalapril followed by an intratracheal dose of BIO1211, there was .apprx.2.5-fold decrease in the AUC of BIO1588 and a 2.4-fold increase in its plasma half-life.

IT INDEXING IN PROGRESS
IT 187735-94-0, BIO1211
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(enalapril effect on peptidyl cleavage of VLA-4 antagonist BIO1211)
RN 187735-94-0 CAPLUS
CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1292873 CAPLUS
DOCUMENT NUMBER: 146:206619
TITLE: Structure-activity relationship studies of a series of peptidomimetic ligands for α4β1 integrin on Jurkat T-leukemia cells
AUTHOR(S): Liu, Ruiwu; Peng, Li; Han, Huijun; Lam, Kit S.
CORPORATE SOURCE: Division of Hematology and Oncology, Department of Internal Medicine, UC Davis Cancer Center, University of California Davis, Sacramento, CA, 95817, USA
SOURCE: Biopolymers (2006), 84(6), 595-604
CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:206619
GI

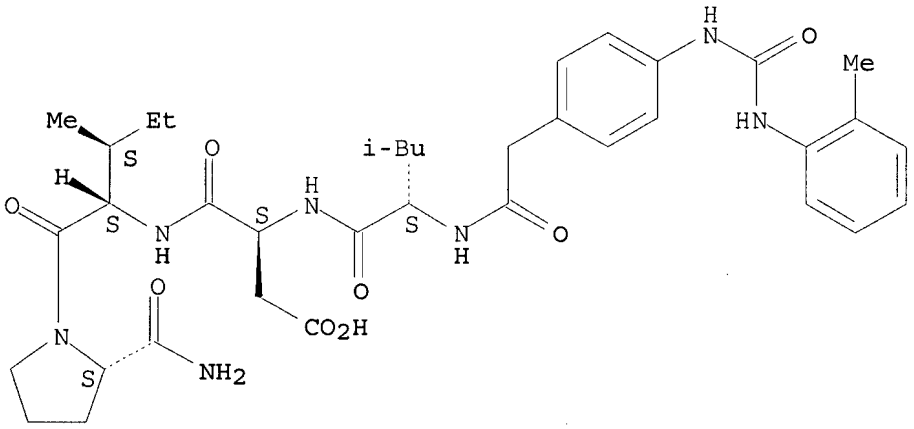
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB α4β1 Integrin is a therapeutic target for inflammation, autoimmune diseases, and lymphoid cancers. A series of peptidomimetic ligands based on the Nle-D-I motif have been synthesized and their binding affinities (IC50) to activated α4β1 integrin on Jurkat T-leukemia cells were determined using a cell adhesion assay. One of the 51 ligands, peptide I, has an IC50 = 0.6 nM, more than two fold increase of binding affinity than the initial lead compound II. Extensive SAR studies provided important information for further ligand optimization, which has served as a foundation for studies that ultimately led to identification of a potent ligand with an IC50 = 2 pM.

IT 922716-39-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase preparation and structure-activity relationships of peptides as ligands of α4β1 integrin)

RN 922716-39-0 CAPLUS
CN L-Prolinamide, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-isoleucyl- (CA INDEX NAME)

Absolute stereochemistry.



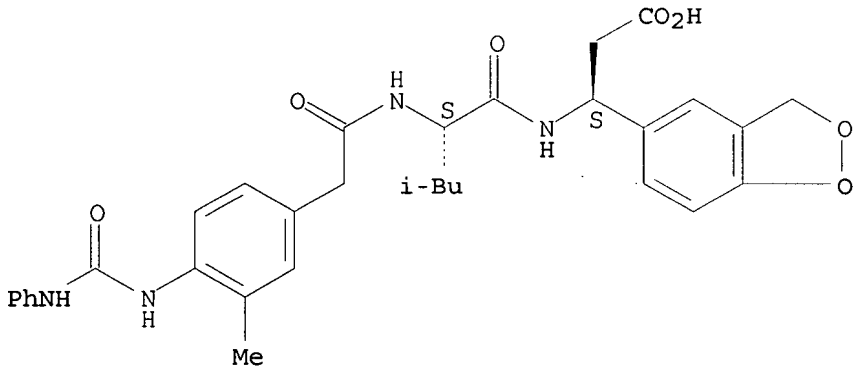
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:324277 CAPLUS
DOCUMENT NUMBER: 142:390938
TITLE: Anti-integrin α4β1 antibodies and ligands for altering hematopoietic progenitor cell adhesion, differentiation, and migration
INVENTOR(S): Varner, Judith A.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005033275	A2	20050414	WO 2004-US31825	20040928
WO 2005033275	A3	20070104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004278748	A1	20050414	AU 2004-278748	20040928
CA 2545248	A1	20050414	CA 2004-2545248	20040928
EP 1685236	A2	20060802	EP 2004-789173	20040928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007509042	T	20070412	JP 2006-534024	20040928
PRIORITY APPLN. INFO.:			US 2003-507202P P	20030929
			WO 2004-US31825 W	20040928

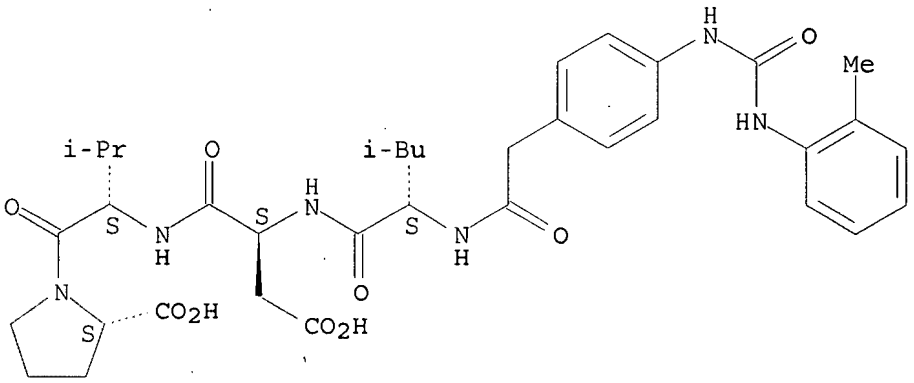
AB The present invention satisfies the need in the art by providing methods for altering hematopoietic progenitor cell adhesion and/or migration to a target tissue. The target tissue is an injured, ischemic and/or malignant vascular endothelium, muscle, neuron, tumor, peripheral blood, cord blood,

Absolute stereochemistry.

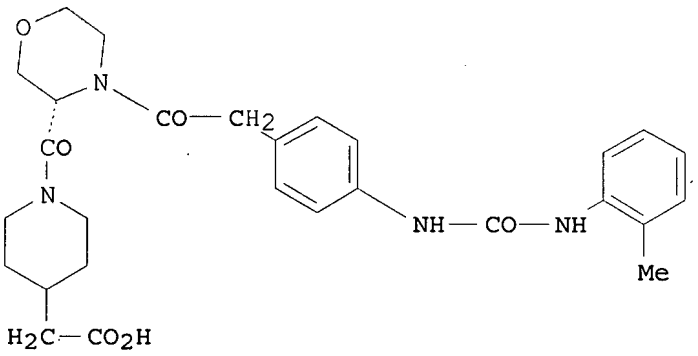


L7 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:86537 CAPLUS
DOCUMENT NUMBER: 143:431977
TITLE: Identified a morpholinyl-4-piperidinylacetic acid derivative as a potent oral active VLA-4 antagonist. [Erratum to document cited in CA142:085870]
AUTHOR(S): Chiba, Jun; Machinaga, Nobuo; Takashi, Tohru; Ejima, Akio; Takayama, Gensuke; Yokoyama, Mika; Nakayama, Atsushi; Baldwin, John J.; McDonald, Edward; Moriarty, Kevin J.; Sarko, Christopher R.; Saionz, Kurt W.; Swanson, Robert; Hussain, Zahid; Wong, Angela
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd., Edogawa-ku, Tokyo, 134-8630, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(4), 1259
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Kevin J. Moriarty and Christopher R. Sarko are added as the tenth and eleventh authors; they are both affiliated with Pharmacopeia Drug Discovery, Inc., Princeton, New Jersey, USA. The correct author list is given.
IT 187735-94-0, Bio-1211
RL: PAC (Pharmacological activity); BIOL (Biological study)
(morpholinyl-4-piperidinylacetic acid derivative as potent oral active VLA-4 antagonist (Erratum))
RN 187735-94-0 CAPLUS
CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1068245 CAPLUS
DOCUMENT NUMBER: 142:85870
TITLE: Identified a morpholinyl-4-piperidinylacetic acid derivative as a potent oral active VLA-4 antagonist
AUTHOR(S): Chiba, Jun; Machinaga, Nobuo; Takashi, Tohru; Ejima, Akio; Takayama, Gensuke; Yokoyama, Mika; Nakayama, Atsushi; Baldwin, John J.; McDonald, Edward; Saionz, Kurt W.; Swanson, Robert; Hussain, Zahid; Wong, Angela
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd., Edogawa-ku, Tokyo, 134-8630, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(1), 41-45
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:85870
GI



I

AB An investigation into the structure-activity relationship of a lead compound, prolyl-5-aminopentanoic acid, led to the identification of a novel series of 4-piperidinylacetic acid, 1-piperazinylacetic acid, and 4-aminobenzoic acid derivs. as potent VLA-4 antagonists with low nanomolar

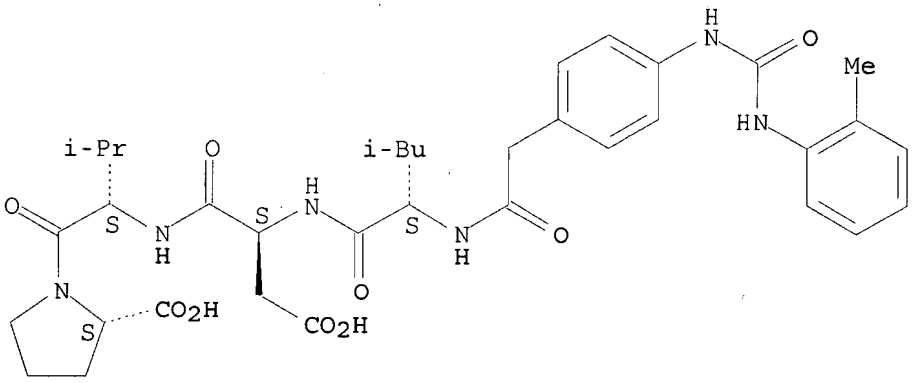
IC50 values. A representative compound morpholinyl-4-piperidinylacetic acid derivative (I: IC50 = 4.4 nM) showed efficacy in the Ascaris antigen-sensitized murine airway inflammation model by oral administration.

IT 187735-94-0, Bio-1211
RL: PAC (Pharmacological activity); BIOL (Biological study)
(morpholinyl-4-piperidinylacetic acid derivative as potent oral active VLA-4 antagonist)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1019870 CAPLUS
DOCUMENT NUMBER: 142:677
TITLE: Ig Fc fragment-linked biologically active molecules for the inhibition of drug binding to serum albumin
INVENTOR(S): Bitonti, Alan J.; Palombella, Vito J.; Stattel, James M.; Peters, Robert T.
PATENT ASSIGNEE(S): Syntonix Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100882	A2	20041125	WO 2004-US14065	20040506
WO 2004100882	A3	20070531		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA

AU 2004238263	A1	20041125	AU 2004-238263	20040506
CA 2522690	A1	20041125	CA 2004-2522690	20040506
US 2005037947	A1	20050217	US 2004-841949	20040506
EP 1624846	A2	20060215	EP 2004-751454	20040506

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.: US 2003-469603P P 20030506
WO 2004-US14065 W 20040506

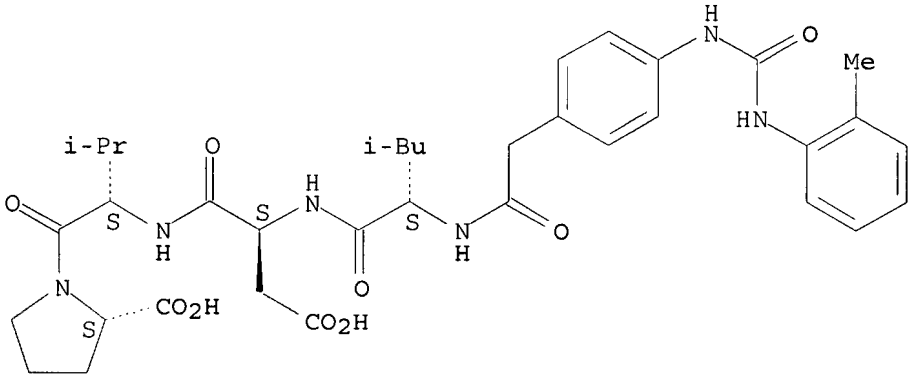
AB The invention relates to improved therapeutics for treating diseases or conditions that provide greater bioavailabilty and more predictable dosing. The invention relates to a chimeric protein comprised of a biol. active mol. linked to an Fc fragment of an Ig, wherein the chimeric protein binds less serum albumin compared to the same biol. active mol. of the chimeric protein not linked to an Fc fragment of an Ig. The invention also relates to a method of treating a disease or condition, the method comprising administering a chimeric protein comprising a biol. active mol. linked to an Fc fragment of an Ig, wherein the chimeric protein binds less serum albumin compared to the same biol. active mol. of the chimeric protein not linked to an Fc fragment of an Ig. Compound preparation (e.g. SYN00534-Fc) is included.

IT 187735-94-0, Bio 1211
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Ig Fc fragment-linked biol. active mols. for inhibition of drug binding to serum albumin)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2004:582909 CAPLUS
DOCUMENT NUMBER:	141:218310
TITLE:	Insights into Phenylalanine Derivatives Recognition of VLA-4 Integrin: From a Pharmacophoric Study to 3D-QSAR and Molecular Docking Analyses
AUTHOR(S):	Macchiarulo, Antonio; Costantino, Gabriele; Meniconi, Mirco; Pleban, Karin; Ecker, Gerhard; Bellocchi, Daniele; Pellicciari, Roberto
CORPORATE SOURCE:	Dipartimento di Chimica e Tecnologia del Farmaco, Universita di Perugia, Perugia, 06127, Italy
SOURCE:	Journal of Chemical Information and Computer Sciences (2004), 44(5), 1829-1839 CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER:	American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English

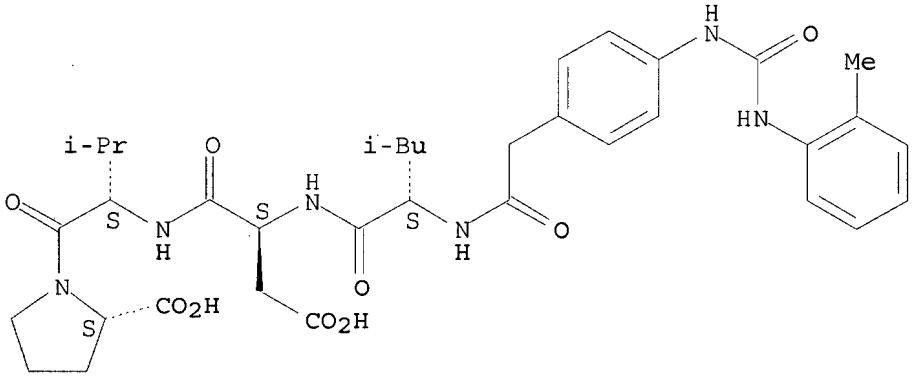
AB The very late antigen-4 (VLA-4), also known as integrin α4β1, is expressed on monocytes, T- and B-lymphocytes, basophils, and eosinophils and is involved in the massive recruitment of granulocytes in different pathol. conditions such as multiple sclerosis and asthma. VLA-4 interacts with its endogenous ligand VCAM-1 during chronic inflammation, and blockade of VLA-4 /VCAM-1 interaction is a potential target for immunosuppression. Two classes of VLA-4 antagonists have so far been reported: β-amino acid derivs. containing a diaryl urea moiety (BIO-1211) and phenylalanine derivs. (TR-14035). With the aim of clarifying the structural basis responsible for VLA-4 recognition by phenylalanine derivs., the authors developed a combined computational study on a set of 128 antagonists available through the literature. Our computational approach is composed of three parts. (i) A VCAM-1 based pharmacophore was constructed with a restricted number of phenylalanine derivs. to identify the region of the protein that resembles synthetic antagonists. The pharmacophore was instrumental in constructing an alignment of a set of 128 compds. This alignment was exploited to build a pseudoreceptor model with the RECEPTOR program. (ii) 3D-QSAR anal. was carried out on the computed electrostatic and steric interaction energies with the pseudoreceptor surface. The 3D-QSAR anal. yielded a predictive model able to explain much of the variance of the 128 antagonists. (iii) A homol. modeling study of the headpiece of VLA-4 based on the crystal structure of αvβ3 was performed. Docking expts. of TR-14035 into the binding site of VLA-4 aided the interpretation of the 3D-QSAR model. The obtained results will be fruitful for the design of new potent and selective antagonists of VLA-4.

IT 187735-94-0, Bio-1211
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3D-QSAR and mol. docking analyses of phenylalanine derivs. recognition of VLA-4 integrin)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.

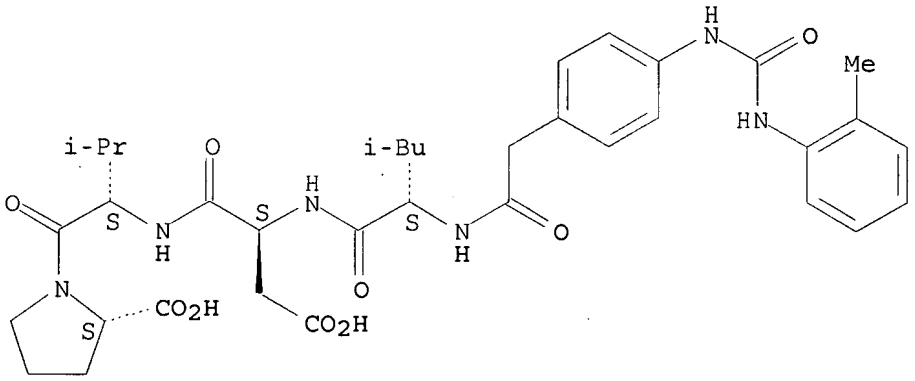


REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:559787 CAPLUS
DOCUMENT NUMBER: 142:68815
TITLE: Effects of BIO-1211 on eosinophil chemotaxis, recruitment and mediator release

AUTHOR(S): Zhao, Xiaoyan; Chen, Jiqiang; Xie, Qiangmin; Tang, Huifang; Bian, Rulian
CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory of State Food and Drug Administration of China ,College of Medicine, Zhejiang University, Hangzhou, 310031, Peop. Rep. China
SOURCE: Zhejiang Daxue Xuebao, Yixueban (2003), 32(4), 279-282, 291
CODEN: ZDXYA9; ISSN: 1008-9292
PUBLISHER: Zhejiang Daxue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effects of very late antigen (VLA) antagonist BIO-1211 on eosinophil chemotaxis, recruitment and mediator release are studied. Eosinophil chemotaxis was induced by platelet activating factor (PAF) in vitro, and eosinophil recruitment and release were determined in vivo. VLA antagonist BIO-1211 inhibits eosinophil chemotaxis induced by PAF. The inhibitory rates at 4 X 10-11, 4 X 10-10, 4 X 10-9 mal/L are 24.9, 29.9 and 31.3%, resp. Pretreatment by BIO-1211 (1, 3 and 10 mg/kg, i.p.) inhibited the recruitment of eosinophils in PAF in sephadex induced rat in a dose-dependent manner, and the inhibitory rates are 60.3, 68.9 and 72.9%, resp. BIO-1211 can not inhibit eosinophil peroxidase (EPO) release from eosinophils. BIO-1211 inhibits eosinophil chemotaxis and recruitment, and alleviates local inflammation, and may represent a new type of drug for allergic diseases.
IT 187735-94-0, BIO-1211
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of BIO-1211 on eosinophil chemotaxis, recruitment and mediator release)
RN 187735-94-0 CAPLUS
CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:559785 CAPLUS
DOCUMENT NUMBER: 142:253303
TITLE: Research on the mechanism of asthma and the development of new drugs
AUTHOR(S): Chen, Jiqiang; Bian, Rulian
CORPORATE SOURCE: Zhejiang Respiratory Drugs Research Laboratory of State, Food and Drug Administration of China, College of Medicine, Zhejiang University, Hangzhou, 310031, Peop. Rep. China

SOURCE: Zhejiang Daxue Xuebao, Yixueban (2003), 32(4), 269-273
CODEN: ZDXYA9; ISSN: 1008-9292
PUBLISHER: Zhejiang Daxue Chubanshe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

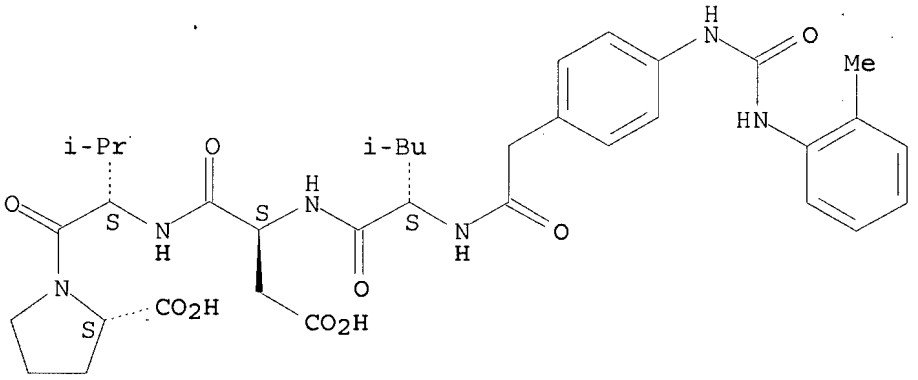
AB A review with 27 refs. on the mechanism of asthma and the development of new drugs with emphases on asthma as chronic airway inflammation and the development of new drugs including ciclamilast, BIO-1211 and a chinese medicine composed of polysaccharides from cryptoporus volvatus.

IT 187735-94-0, BIO-1211
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(research on mechanism of asthma and the development of new drugs)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

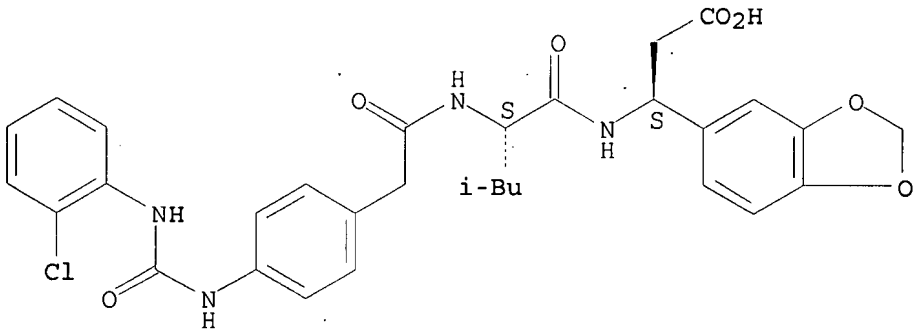
ACCESSION NUMBER: 2002:813789 CAPLUS
DOCUMENT NUMBER: 138:280734

TITLE: 3D QSAR (COMFA) of a series of potent and highly selective VLA-4 antagonists

AUTHOR(S): Singh, Juswinder; Van Vlijmen, Herman; Lee, Wen-Cherng; Liao, Yusheng; Lin, Ko-Chung; Ateeq, Humayun; Cuervo, Julio; Zimmerman, Craig; Hammond, Charles; Karpusas, Michael; Palmer, Rex; Chattopadhyay, Tapan; Adams, Steven P.
CORPORATE SOURCE: Biogen Inc, Cambridge, MA, 02142, USA

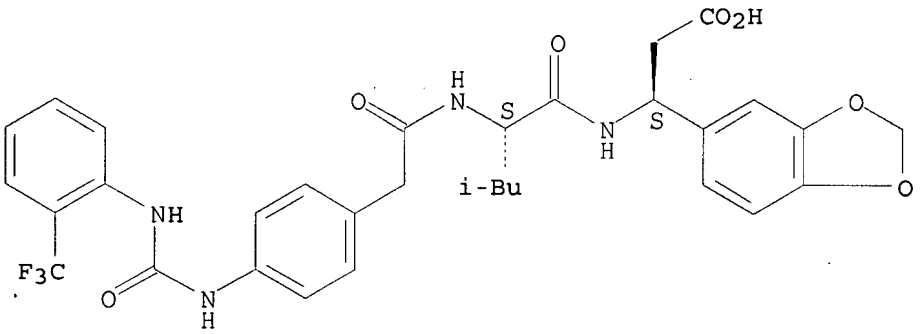
SOURCE: Journal of Computer-Aided Molecular Design (2002), 16(3), 201-211
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The integrin VLA-4 (α4β1) is involved in the migration of white blood cells to sites of inflammation, and is implicated in the pathol. of a variety of diseases including asthma and multiple sclerosis. We report the structure-activity relationships of a series of VLA-4 antagonists that were based upon the integrin-binding sequence of the connecting segment peptide of fibronectin (Leu-Asp-Val), and of VCAM-1 (Ile-Asp-Ser), both natural ligands of VLA-4. We explore variation in the ligand derived peptide portion of these antagonists and also in the novel N-terminal cap, which have discovered through chemical optimization, and which confers high affinity and selectivity. Using the x-ray derived conformation of the



RN 505082-16-6 CAPLUS
CN β-Alanine, N-[[4-[[[[2-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-3-(1,3-benzodioxol-5-yl)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:434328 CAPLUS
DOCUMENT NUMBER: 137:163322
TITLE: Identification of Potent and Novel α4β1 Antagonists Using in Silico Screening
AUTHOR(S): Singh, Juswinder; van Vlijmen, Herman; Liao, Yusheng; Lee, Wen-Cherng; Cornebise, Mark; Harris, Mary; Shu, I-hsiang; Gill, Alan; Cuervo, Julio H.; Abraham, William M.; Adams, Steven P.
CORPORATE SOURCE: Department of Drug Design and Evaluation, Biogen Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(14), 2988-2993
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:163322
AB The antigen α4β1 (very late antigen-4, VLA-4) plays an important role in the migration of white blood cells to sites of inflammation. It has been implicated in the pathol. of a variety of diseases including asthma, multiple sclerosis, and rheumatoid arthritis. The authors describe a series of potent inhibitors of α4β1 that were discovered using computational screening for replacements of the peptide region of an existing tetrapeptide-based α4β1 inhibitor

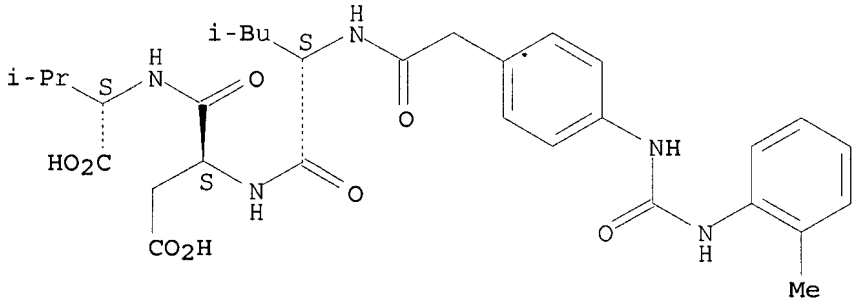
(4-[N'-(2-methylphenyl)ureido]phenylacetyl-Leu-Asp-Val) (I) derived from fibronectin. The search query was constructed using a model of I that was based upon the x-ray conformation of the related integrin-binding region of vascular cell adhesion mol.-1 (VCAM-1). The 3D search query consisted of the N-terminal cap and the carboxyl side chain of I because, upon the basis of existing structure-activity data on this series, these were known to be critical for high-affinity binding to α4β1. The computational screen identified 12 reagents from a virtual library of 8624 mols. as satisfying the model and the authors synthetic filters. All of the synthesized compds. tested inhibit α4β1 association with VCAM-1, with the most potent compound having an IC50 of 1 nM, comparable to the starting compound Using CATALYST, a 3D QSAR was generated that rationalizes the variation in activities of these α4β1 antagonists. The most potent compound was evaluated in a sheep model of asthma, and a 30 mg nebulized dose was able to inhibit early and late airway responses in allergic sheep following antigen challenge and prevented the development of nonspecific airway hyperresponsiveness to carbachol. Our results demonstrate that it is possible to rapidly identify nonpeptidic replacements of integrin peptide antagonists. This approach should be useful in identification of nonpeptidic α4β1 inhibitors with improved pharmacokinetic properties relative to their peptidic counterparts.

IT 187737-40-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of potent and novel α4β1 antagonists using in silico screening in relation to asthma treatment)

RN 187737-40-2 CAPLUS

CN L-Valine, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:336120 CAPLUS

DOCUMENT NUMBER: 137:288800

TITLE: Pulmonary eosinophilia in a murine model of allergic inflammation is attenuated by small molecule α4β1 antagonists

AUTHOR(S): Kudlacz, E.; Whitney, C.; Andresen, C.; Duplantier, A.; Beckius, G.; Chupak, L.; Klein, A.; Kraus, K.; Milici, A.

CORPORATE SOURCE: Pfizer Global Research and Development, Groton, CT, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 301(2), 747-752
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

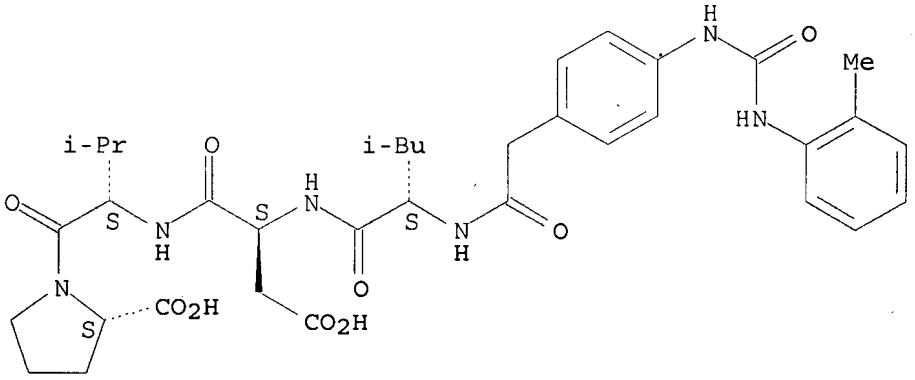
AB Inhibition of α4β1/vascular cell adhesion mol.-1 (VCAM-1) interactions have therapeutic potential in treating allergic airway disease because of the importance of these adhesion mols. in the trafficking of eosinophils, lymphocytes, and monocytes. The authors examined several small mol. inhibitors of α4β1/VCAM-1 interactions with in vitro potencies (IC50 values) ranging from 0.52 nM (CP-664511; 3-[3-(1-{2-[3-methoxy-4-(3-O-tolyl-ureido)phenyl]-acetylamino}-3-methyl-butyl)isoxazol-5-yl]-propionic acid) to 38.5 nM (CP-609643; 3-[3-(3-methyl-1-{2-[4-(3-O-tolyl-ureido)-phenyl]-acetylamino}-butyl)-isoxazol-5-yl]-propionic acid). The same compds. were evaluated in vivo using a murine model of ovalbumin-induced pulmonary eosinophilia. In this model, systemic administration of antibodies against α4 reduced bronchoalveolar lavage (BAL) eosinophilia .apprx.60%. Small mol. α4β1 antagonists were administered by intratracheal instillation and demonstrated dose-dependent inhibition of BAL eosinophil nos. and achieved a maximum inhibition of .apprx.60%. In general, the rank order of potency for these compds. in vitro was consistent with that observed in vivo, which confirms that their efficacy is likely via blockade of α4β1/VCAM-1 interactions. The most potent compound, CP-664511, also inhibited BAL eosinophilia following s.c. administration (1-10 mg/kg, s.c.). These data support the utility of small mol. α4β1 antagonists in the treatment of relevant diseases, such as asthma.

IT 187735-94-0, BIO1211
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pulmonary eosinophilia in murine model of allergic inflammation is attenuated by small mol. α4β1 antagonists)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

inventors

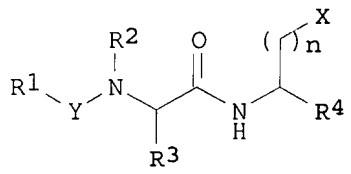
L7 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:312019 CAPLUS
DOCUMENT NUMBER: 136:325828
TITLE: Preparation of dipeptide derivatives as cell adhesion inhibitors
INVENTOR(S): Adams, Steven P.; Lin, Ko-Chung; Lee, Wen-Cherng; Castro, Alfredo C.; Zimmerman, Craig N.; Hammond,

Charles E.; Liao, Yu-Sheng; Cuervo, Julio Hernan; Singh, Juswinder
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: U.S., 50 pp., Cont.-in-part of U.S. 6,306,840.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

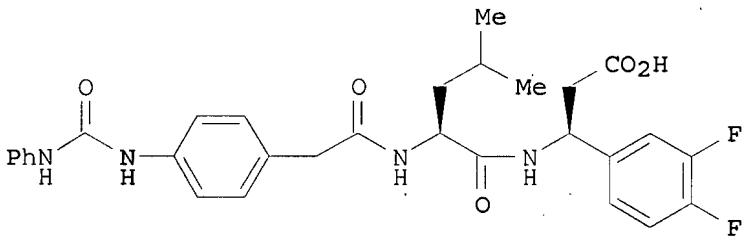
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6376538	B1	20020423	US 1997-875321	19970919
US 6306840	B1	20011023	US 1995-376372	19950123
WO 9622966	A1	19960801	WO 1996-US1349	19960118
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
EP 1142867	A2	20011010	EP 2001-107877	19960118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
AU 766538	B2	20031016	AU 2000-62432	20001002
US 2003018016	A1	20030123	US 2001-2341	20011023
US 6630512	B2	20031007		
US 7001921	B1	20060221	US 2003-625626	20030724
US 2006166866	A1	20060727	US 2003-679478	20031007

PRIORITY APPLN. INFO.:
US 1995-376372 A2 19950123
WO 1996-US1349 W 19960118
AU 1996-49115 A3 19960118
EP 1996-905316 A3 19960118
US 1997-875321 A3 19970919
US 2001-935461 A1 20010822
US 2001-2341 A1 20011023

OTHER SOURCE(S): MARPAT 136:325828
GI

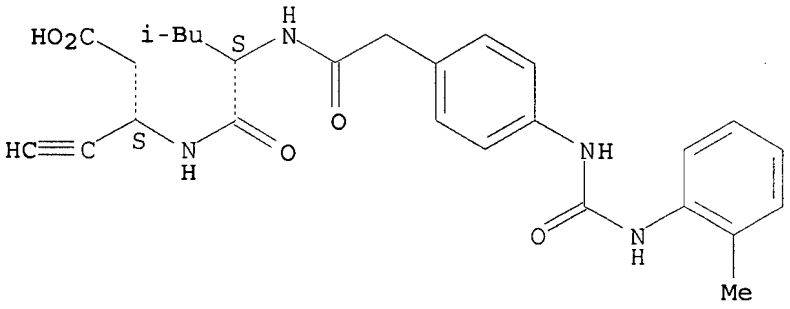


I



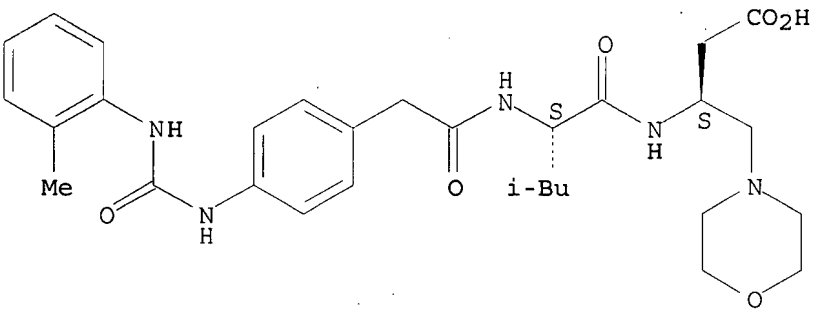
II

AB Novel dipeptide analogs I [X = CO2H, PO3H-, SO2R5, SO3H, OPO3H-, CO2R4; Y = CO, SO2, PO2; n = 0-2; R1 = optionally substituted alkyl, alkenyl, alkynyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl,



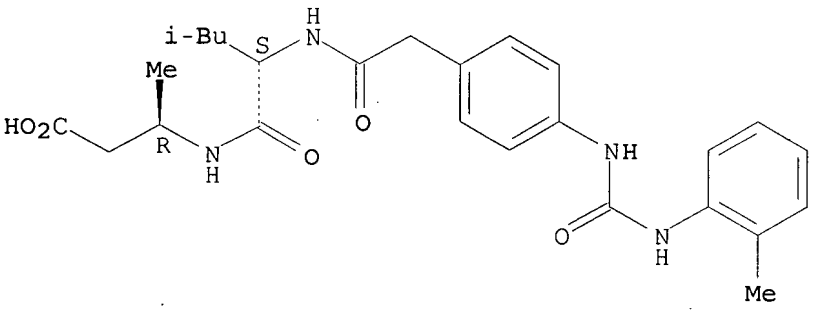
RN 181523-75-1 CAPLUS
CN 4-Morpholinebutanoic acid, β-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 181525-87-1 CAPLUS
CN Butanoic acid, 3-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

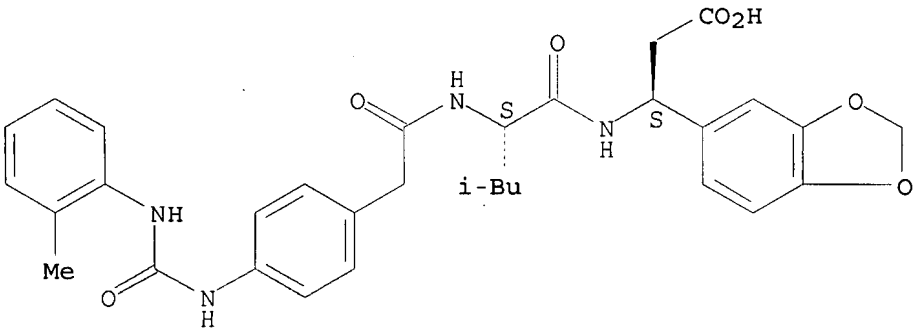


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:780025 CAPLUS
DOCUMENT NUMBER: 136:232102
TITLE: Design and Synthesis of Potent and Selective Inhibitors of Integrin VLA-4
AUTHOR(S): Wattanasin, Sompong; Weidmann, Beat; Roche, Didier;

Myers, Stewart; Xing, Amy; Guo, Qin; Sabio, Michael; von Matt, Peter; Hugo, Ronald; Maida, Susan; Lake, Philip; Weetall, Marla
CORPORATE SOURCE: Novartis Pharmaceuticals Corporation, Novartis Institute for Biomedical Research, Summit, NJ, 07901, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(22), 2955-2958
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:232102
AB The synthesis and identification of a novel series of inhibitors of integrin VLA-4 are described. Their in vitro activity and selectivity against closely related integrins are also presented. The compds. prepared and tested were modeled upon (βS)-β-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-1,3-benzodioxole-5-propanoic acid and (3R)-3-[[(2S)-4-methyl-2-[[[3-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-5-hexenoic acid.
IT 181522-44-1
RL: PAC (Pharmacological activity); BIOL (Biological study)
(design and synthesis of selective integrin VLA-4 inhibitors)
RN 181522-44-1 CAPLUS
CN 1,3-Benzodioxole-5-propanoic acid, β-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:771942 CAPLUS
DOCUMENT NUMBER: 136:226237
TITLE: LC/MS/MS plasma assay for the peptidomimetic VLA4 antagonist I and its major active metabolite II: for treatment of asthma by inhalation
AUTHOR(S): Fisher, Alison L.; DePuy, Elizabeth; Jayaraj, Andrew; Raab, Conrad; Braun, Matt; Ellis-Hutchings, Michel; Zhang, Jin; Rogers, John D.; Musson, Donald G.
CORPORATE SOURCE: WP75A-303, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2002), 27(1-2), 57-71
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.

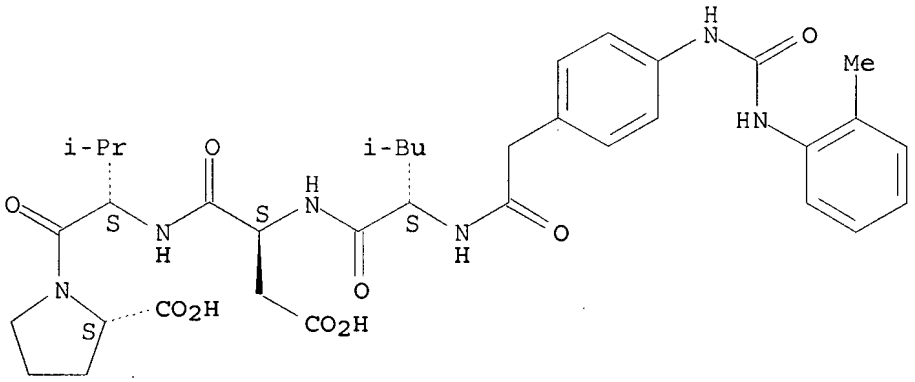
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vitro and in animals, I is a potent and specific peptidomimetic for the potential treatment of airway inflammation in the pathogenesis of asthma. Preclin. studies indicated extensive conversion of I to an active metabolite II, and thus, a very sensitive assay for I and II was needed to support an inhalation ascending-dose study in man. The LC/MS/MS plasma/urine assay method (1.0 mL of sample) involves the following: liquid-liquid extraction of acidified plasma into pentane-EtOAc (90:10 volume/volume); evaporation of the organic extract, reconstitution into MeOH; addition of H2O to the methanolic extract and freezing. After thawing, the extract is centrifuged and the clear supernatant injected for chromatog. Extract is chromatographed on a YMC ODS-AM column (50+2.0 mm). For detection, a Sciex 365 LC/MS/MS with an electrospray inlet and used in the pos. ion, multiple reaction monitoring mode was used to monitor precursor fragment ions of m/z 709,594 for I and m/z 513,380 for II. The plasma assay was linear over the concentration range of 0.1-100 ng/mL in plasma for I and II. Accuracy and precision for I ranged from 97.9 to 102.1% of nominal with a 0.84-10.65% CV; similarly for II, 98.0-101.7% and 1.39-9.28% CV, resp. Extraction recovery averaged 63.7% for I and 64.9% for II. This general assay methodol. may be applied to assay small acidic peptides and peptidomimetics from biol. fluids by LC/MS/MS.

IT 187735-94-0 224577-01-9
RL: ANT (Analyte); ANST (Analytical study)
(LC/MS/MS plasma assay for the peptidomimetic VLA4 antagonist I and its major active metabolite II: for treatment of asthma by inhalation)

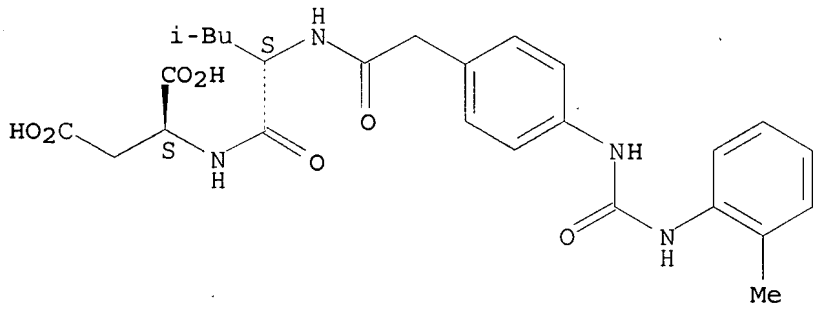
RN 187735-94-0 CAPLUS
CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 224577-01-9 CAPLUS
CN L-Aspartic acid, N-[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:137020 CAPLUS
DOCUMENT NUMBER: 134:193741
TITLE: Preparation of peptide derivatives as cell adhesion inhibitors
INVENTOR(S): Lee, Wen-Cherng; Scott, Daniel; Cornebise, Mark; Petter, Russell
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012186	A1	20010222	WO 2000-US22285	20000814
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2380817	A1	20010222	CA 2000-2380817	20000814
BR 2000013248	A	20020723	BR 2000-13248	20000814
HU 2002002469	A2	20021128	HU 2002-2469	20000814
EP 1265606	A1	20021218	EP 2000-959232	20000814
EP 1265606	B1	20061025		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506491	T	20030218	JP 2001-516532	20000814
EE 200200070	A	20030415	EE 2002-70	20000814
US 6630503	B1	20031007	US 2000-638652	20000814
NZ 517011	A	20040227	NZ 2000-517011	20000814
AU 780610	B2	20050407	AU 2000-70586	20000814
AT 343383	T	20061115	AT 2000-959232	20000814
EP 1741428	A2	20070110	EP 2006-21333	20000814
EP 1741428	A3	20070509		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
ES 2270868	T3	20070416	ES 2000-959232	20000814
IN 2002DN00160	A	20061229	IN 2002-DN160	20020207

MX 2002PA01449	A	20020702	MX 2002-PA1449		20020211
ZA 2002001158	A	20030512	ZA 2002-1158		20020211
NO 2002000725	A	20020408	NO 2002-725		20020213
NO 324044	B1	20070730			
BG 106510	A	20021031	BG 2002-106510		20020311
HK 1051500	A1	20070202	HK 2003-103786		20030527
US 2004132809	A1	20040708	US 2003-677756		20031003
US 7034043	B2	20060425			
US 2006166961	A1	20060727	US 2006-362043		20060227
PRIORITY APPLN. INFO.:			US 1999-148845P	P	19990813
			EP 2000-959232	A3	20000814
			US 2000-638652	A1	20000814
			WO 2000-US22285	W	20000814
			US 2003-677756	A1	20031003

OTHER SOURCE(S): MARPAT 134:193741

AB Cell adhesion inhibitors of the general formula R3-L-L'-R1 (R1 = H, C1-10alkyl, C2-10alkenyl or -alkynyl, cycloalkyl, cycloalkylalkyl, -alkenyl, or -alkynyl; L' and L are hydrocarbon linker moieties having 1-5 or 1-14 carbons, resp., which are optionally substituted and interrupted by, or terminally attached to, various groups; R3 = alkyl, cycloalkyl, aryl, aralkyl, aryloxy, arylamino, heterocyclyl, etc.) were prepared An inhibitor of the present invention interacts with VLA-4 mols. to inhibit VLA-4 dependent cell adhesion. Thus, N2-[N-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl]-N4-[N-(o-MePUPA)-N-methyl-L-leucyl]-L-2,4-diaminobutyric acid [o-MePUPA = [4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl] was prepared via peptide coupling reactions in solution

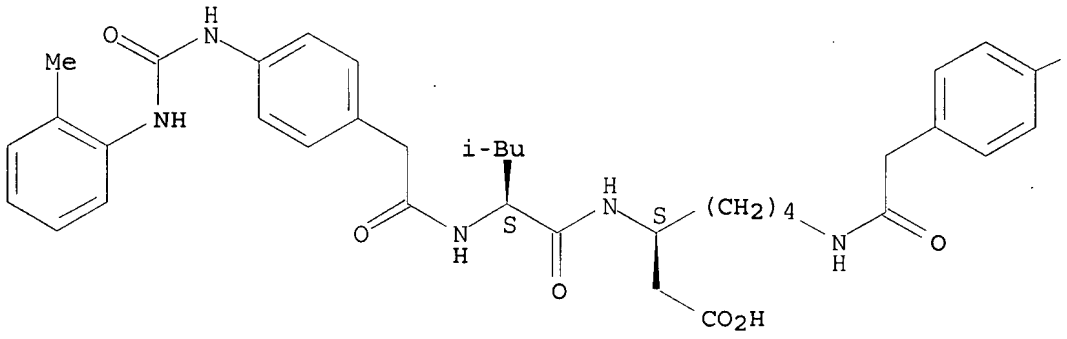
IT 327612-71-5P 327612-72-6P 327612-73-7P
327613-58-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide derivs. as cell adhesion inhibitors)

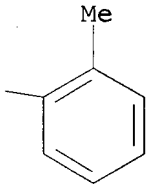
RN 327612-71-5 CAPLUS

CN Heptanoic acid, 3-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-7-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

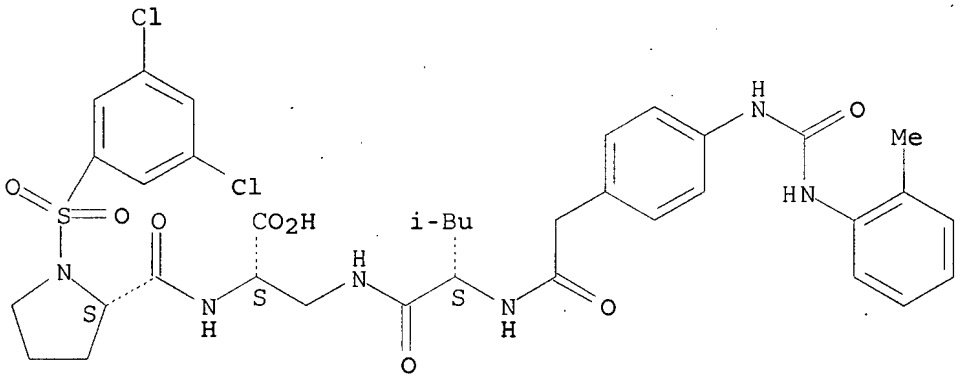
PAGE 1-A





RN 327613-58-1 CAPLUS
CN L-Alanine, 1-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl-3-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:353355 CAPLUS
DOCUMENT NUMBER: 132:342664
TITLE: Bio-1211 (Biogen)
AUTHOR(S): Bolger, Gordon T.
CORPORATE SOURCE: Bio-Mega/Boehringer Ingelheim Research Inc, Lavel, QC, H7S 2G5, Can.
SOURCE: Current Opinion in Anti-Inflammatory and Immunomodulatory Investigational Drugs (2000), 2(2), 108-112
CODEN: COAIFF; ISSN: 1464-8474
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 45 refs. Biogen, in collaboration with Merck & Co, was developing late activator VLA4 (α4β1) integrin antagonists for the potential treatment of inflammatory conditions. Merck carried out a phase IIa trial with the lead compound, BIO-1211, for asthma, but has recently discontinued development due to a lack of efficacy. Biogen is also no longer carrying out clin. studies with BIO-1211 and it is unclear at this time if the drug is still being investigated for any of the other reported indications, although a recent patent application, WO-09961421, suggests that Biogen may still be investigating the potential of this class of drug in inflammatory or immune disorders. Under the collaborative agreement, each company had worldwide rights to certain

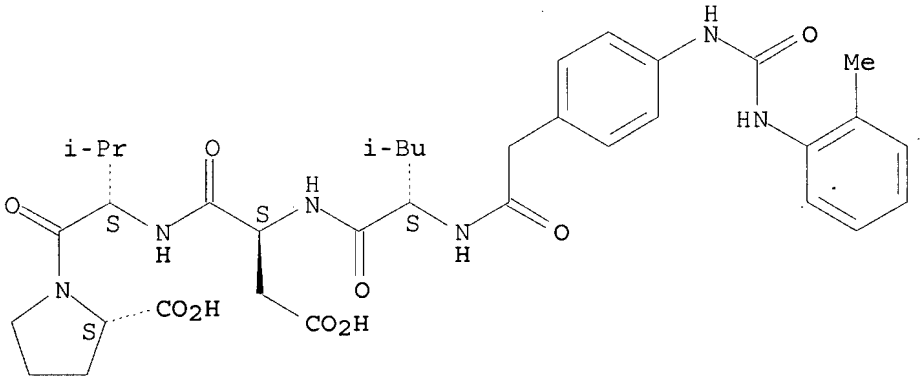
indications; Merck had rights for asthma and Biogen retained the rights to a number of smaller indications including multiple sclerosis, inflammatory bowel disease, renal indications and most diseases in which the US patient population is less than 200,000. VLA4 inhibitors show anti-inflammatory action by inhibition of binding between adhesion factors and leukocytes, but with no loss of basophil function, and they have the advantage of specificity not seen with existing drugs. In Feb. 1999, for the asthma indication (Merck), Lehman Brothers had predicted 40% probabilities that the compound would reach the US and ex-US markets, and launch onto these markets by 2003. Peak annual sales of US $500 million (US) and US $500 million (outside US) were predicted on this basis, both in 2010.

IT 187735-94-0, Bio-1211
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(status of development of anti-inflammatory bio-1211)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:312195 CAPLUS
DOCUMENT NUMBER: 133:26389
TITLE: BIO-1211 Biogen
AUTHOR(S): Bolger, Gordon T.
CORPORATE SOURCE: Bio-Mega/Boehringer Ingelheim Research Inc, Lavel, QC, H7S 2G5, Can.
SOURCE: IDrugs (2000), 3(5), 536-540
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with many refs. is given. Biogen, in collaboration with Merck & Co, is developing late activator VLA-4 (α4β1) integrin antagonists for the potential treatment of inflammatory conditions. Merck has begun phase II trials with the lead compound, BIO-1211, for asthma, Biogen is still conducting preclin. research for its designated indications. Under the collaborative agreement, each company has worldwide rights to certain indications; Merck has rights for asthma and Biogen retains the rights to a number of smaller indications, including multiple sclerosis, inflammatory bowel disease, renal indications and most diseases in which the US patient population is <200,000. VLA-4 inhibitors show anti-inflammatory action by inhibition of binding between adhesion factors and leukocytes, but with no loss of basophil function, and they

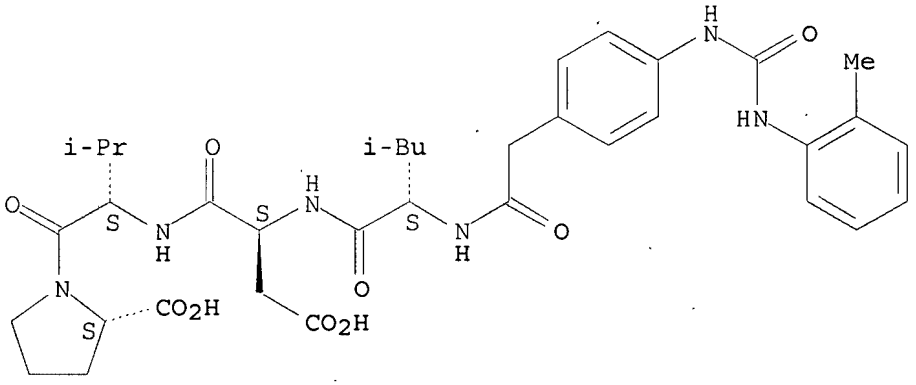
have the advantage of specificity not seen with existing drugs. In Feb. 1999, Lehman Brothers predicted 40% probabilities that the compound would reach the US and ex-US markets for the asthma indication (Merck), and launch onto these markets by 2003. Peak annual sales of US $500 million (US) and US $500 million (outside US) are predicted, both in 2010.

IT 187735-94-0, BIO-1211
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BIO-1211, an antiinflammatory agent)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:317616 CAPLUS

DOCUMENT NUMBER: 131:126890

TITLE: Multiple activation states of integrin α4β1 detected through their different affinities for a small molecule ligand

AUTHOR(S): Chen, Ling Ling; Whitty, Adrian; Lobb, Roy R.; Adams, Steven P.; Pepinsky, R. Blake

CORPORATE SOURCE: Biogen, Inc., Cambridge, MA, 02142, USA

SOURCE: Journal of Biological Chemistry (1999), 274(19), 13167-13175
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have used the highly specific α4β1 inhibitor 4-((N'-2-methylphenyl)ureido)-phenylacetyl-leucine-aspartic acid-valine-proline (BIO1211) as a model LDV-containing ligand to study α4β1 integrin-ligand interactions on Jurkat cells under diverse conditions that affect the activation state of α4β1. Observed KD values for BIO1211 binding ranged from a value of 20-40 nM in the nonactivated state of the integrin that exists in 1 mM Mg2+, 1 mm Ca2+ to 100 pM in the activated state seen in 2 mM Mn2+ to 18 pM when binding was measured after coactivation by 2 mM Mn2+ plus 10 μg/mL of the integrin-activating monoclonal antibody TS2/16. The large range in KD values was governed almost exclusively by differences in the dissociation rates of the integrin-BIO1211 complex, which ranged from 0.17 x 10-4 s-1 to >140 x 10-4 s-1. Association rate consts. varied only slightly under the same conditions, all falling in the narrow range from 0.9 to 2.7 x 106 M-1

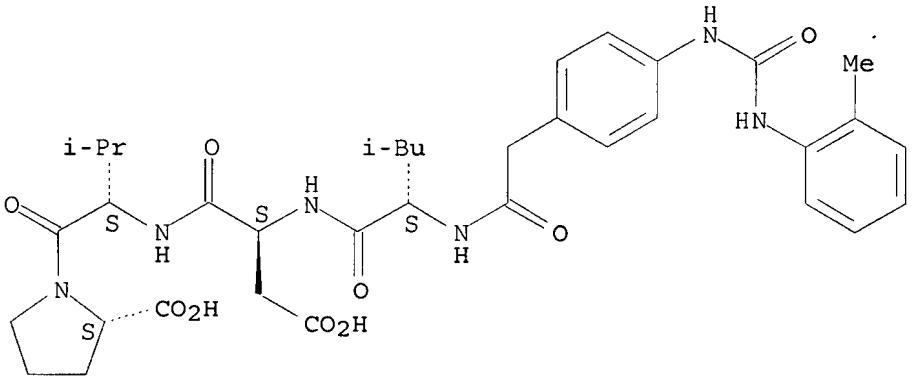
s-1. The further increase in affinity observed upon co-activation by divalent cations and TS2/16 compared with that observed at saturating concns. of metal ions or TS2/16 alone indicates that the mechanism by which these factors bring about activation are distinct and identified a previously unrecognized high affinity state on α4β1, that had not been detected by conventional assay methods. Similar changes in affinity were observed when the binding properties of vascular cell adhesion mol.-1 and CS1 to α4β1 were studied, indicating that the different affinity states detected with BIO1211 are an inherent property of the integrin.

IT 187735-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(multiple activation states of integrin α4β1 detected through different affinities for small mol. ligand)

RN 187735-94-0 CAPLUS

CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:161426 CAPLUS

DOCUMENT NUMBER: 130:332268

TITLE: Selective, Tight-Binding Inhibitors of Integrin α4β1 That Inhibit Allergic Airway Responses

AUTHOR(S): Lin, Ko-chung; Ateeq, Humayun S.; Hsiung, Sherry H.; Chong, Lillian T.; Zimmerman, Craig N.; Castro, Alfredo; Lee, Wen-cherng; Hammond, Charles E.; Kalkunte, Sandhya; Chen, Ling-Ling; Pepinsky, R. Blake; Leone, Diane R.; Sprague, Andrew G.; Abraham, William M.; Gill, Alan; Lobb, Roy R.; Adams, Steven P.

CORPORATE SOURCE: Biogen Inc., Cambridge, MA, 02142, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(5), 920-934
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Integrin α4β1 mediates leukocyte recruitment, activation, mediator release, and apoptosis inhibition, and it plays a central role in inflammatory pathophysiol. High-affinity, selective inhibitors of α4β1, based on the Leu-Asp-Val (LDV) sequence from the alternatively spliced connecting segment-1 (CS-1) peptide of cellular fibronectin, are described that employ a novel N-terminal peptide "cap"

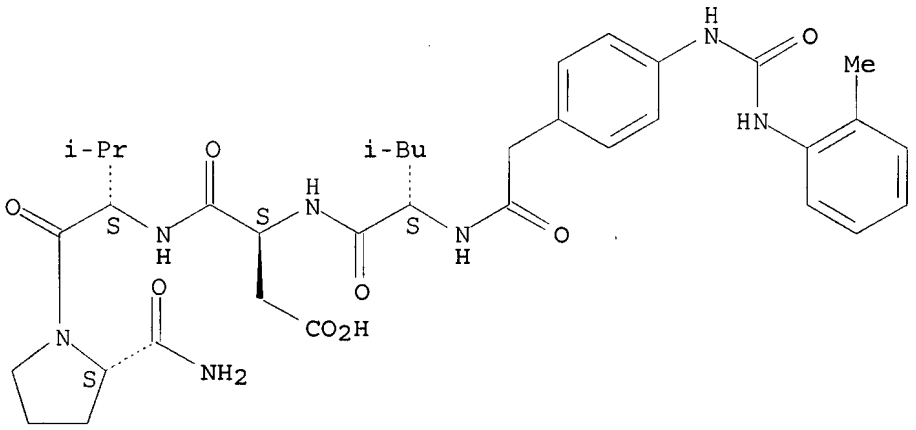
strategy. One inhibitor, BIO-1211, was .apprx.106-fold more potent than the starting peptide and exhibited tight-binding properties (koff = 1.4 + 10-4 s-1, KD = 70 pM), a remarkable finding for a noncovalent, small-mol. inhibitor of a protein receptor. BIO-1211 was also 200-fold selective for the activated form of α4β1, and it stimulated expression of ligand-induced epitopes on the integrin β1 subunit, a property consistent with occupancy of the receptor's ligand-binding site. Pretreatment of allergic sheep with a 3-mg nebulized dose of BIO-1211 inhibited early and late airway responses following antigen challenge and prevented development of nonspecific airway hyperresponsiveness to carbachol. These results show that highly selective and potent small-mol. antagonists can be identified to integrins with primary specificity for peptide domains other than Arg-Gly-Asp (RGD); they confirm the generality of integrins as small mol. targets; and they validate α4β1 as a therapeutic target for asthma.

IT 187735-36-0 187735-91-7 187735-94-0
187737-31-1 187737-40-2 224577-01-9
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(synthesis of integrin α4β1 inhibitors that inhibit allergic airway responses)

RN 187735-36-0 CAPLUS

CN L-Prolinamide, N-[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (9CI) (CA INDEX NAME)

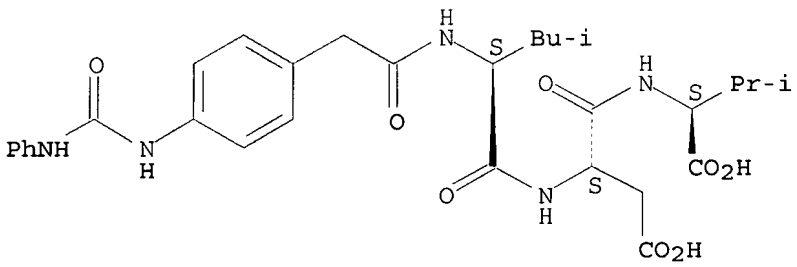
Absolute stereochemistry.

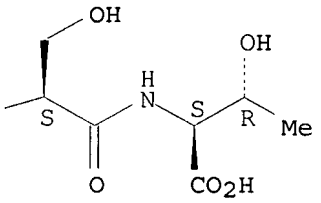


RN 187735-91-7 CAPLUS

CN L-Valine, N-[[4-[[(phenylamino)carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl- (9CI) (CA INDEX NAME)

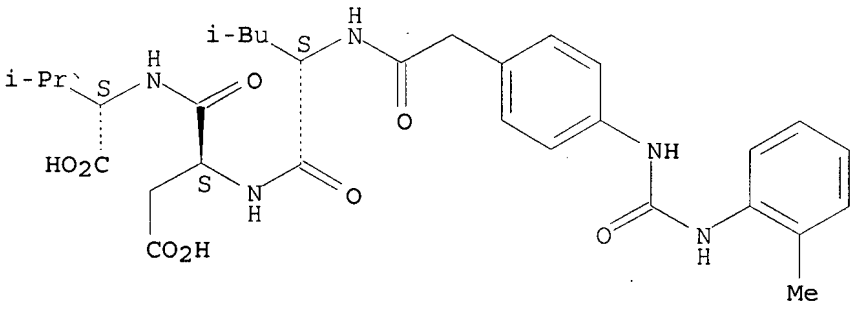
Absolute stereochemistry.





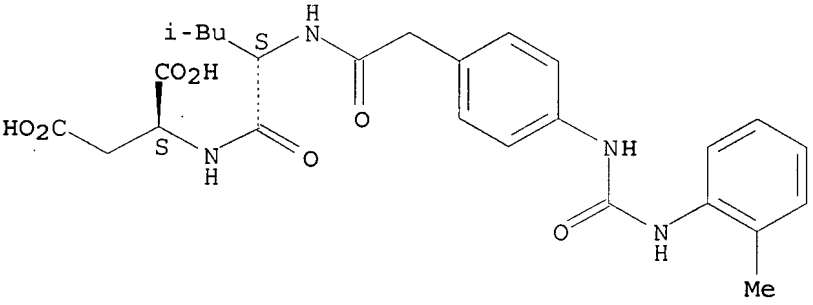
RN 187737-40-2 CAPLUS
CN L-Valine, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 224577-01-9 CAPLUS
CN L-Aspartic acid, N-[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

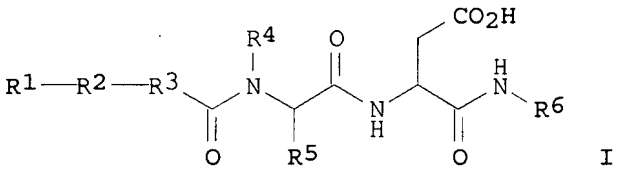
L7 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:677800 CAPLUS
DOCUMENT NUMBER: 129:276355

10/679,478

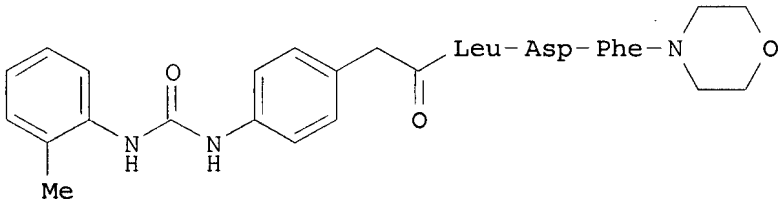
TITLE: Preparation of peptides and peptidomimetics as VLA-4 antagonists
INVENTOR(S): He, Ya-Bo; Elices, Mariano J.; Arrhenius, Thomas S.
PATENT ASSIGNEE(S): Cytel Corporation, USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842656	A1	19981001	WO 1998-US5709	19980320
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1997-821825 A	19970321
OTHER SOURCE(S):	MARPAT 129:276355			

GI



I



II

AB Title compds. I [R1 = alkyl, adamantyl, (un)substituted non-heterocyclic, heterocyclic, aromatic, or partially or fully saturated ring; R2 = lower alkyl, alkenyl, or alkynyl group in which each group optionally can contain a carbonyl, ether, thioether, aminocarbonyl group, etc., or E-C(R7)-F where R7 = S, O; E = CX1X2, NX3, or O; F = CX4X5, NX6, or O; X1-X6 = independently H or a lower alkyl, with the proviso that E and F are not simultaneously oxygen atoms and if R1 is an alkyl group, R2 must be of formula E-C(R7)-F; R3 = 5-, 6-, 6,5-, or 6,6- membered aromatic ring optionally containing 1-3 heteroatoms selected from the group O, N, S; R4 = H, lower alkyl; R5 = H, lower alkyl, (un)substituted lower alkyl amido group, or a 5- or 6- membered non-heterocyclic saturated ring connected directly by a bond or through a lower alkyl group; R6 = substituted azepine, or CH(R8)COAR9R10 where A = N, O; R8 = H, lower alkyl, hydroxyalkyl, thioalkyl, a ring structure connected directly by a bond or through a lower alkyl group, or R8 and R9 together form a ring structure, etc.; R9 = lower alkyl, hydroxyalkyl, morpholino group, or together with R10 form a ring structure; R10 = (un)substituted lower alkyl, or together with R9 form a ring structure; when A = O, R10 is absent] and pharmaceutically-acceptable derivs. thereof. were prepared as VLA-4 antagonists. Thus, II (solution phase preparation given) was assayed for binding inhibition potency (IC50 = 0.4 nM) toward Jurkat cells.

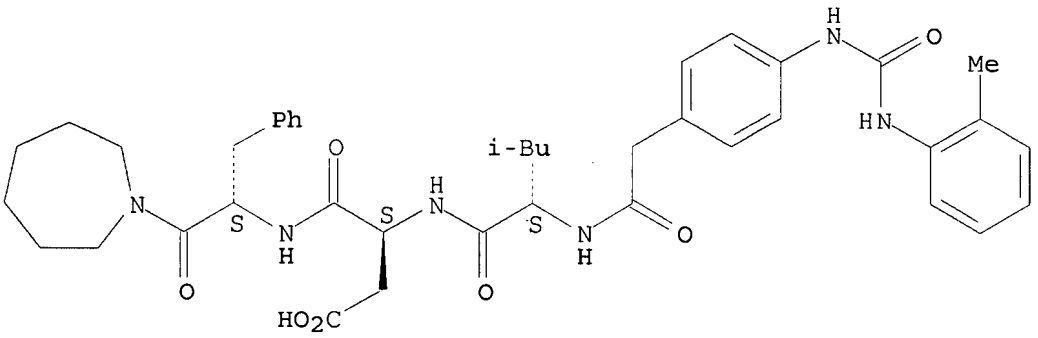
IT 213989-63-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of peptides and peptidomimetics as VLA-4 antagonists)

RN 213989-63-0 CAPLUS

CN L-α-Asparagine, N-[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-N-[(1S)-2-(hexahydro-1H-azepin-1-yl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 213989-21-0P 213989-23-2P 213989-27-6P
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213989-40-3P 213989-41-4P 213989-42-5P
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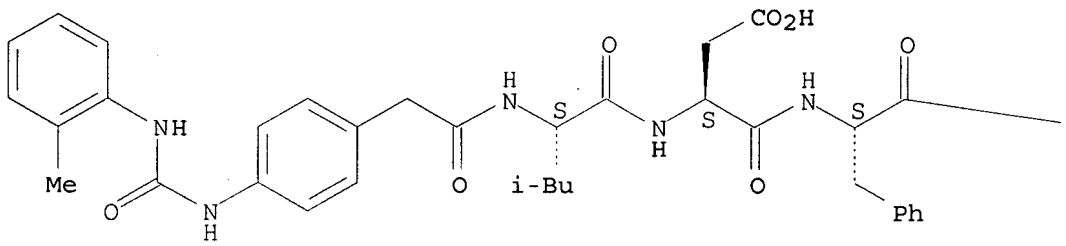
213989-75-4P 213989-77-6P 213989-87-8P
213989-88-9P 213990-01-3P 213990-08-0P
213990-09-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides and peptidomimetics as VLA-4 antagonists)

RN 213989-21-0 CAPLUS

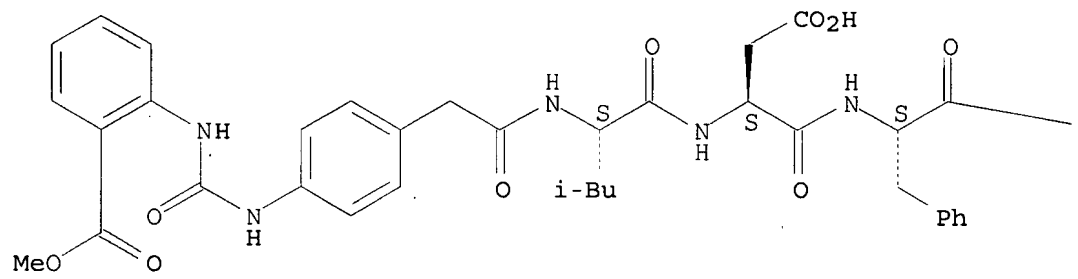
CN L-α-Asparagine, N-[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-N-[(1S)-2-(4-morpholinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

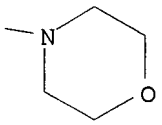
PAGE 1-A



PAGE 1-A

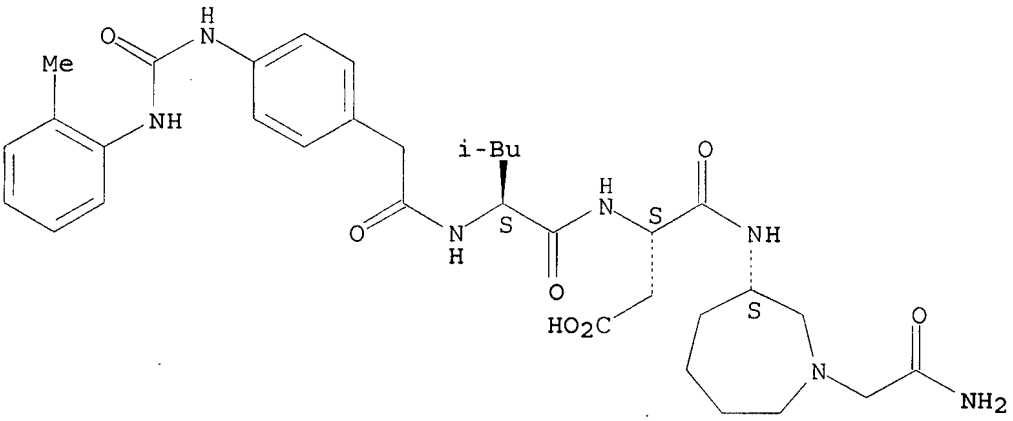


PAGE 1-B



RN 213990-09-1 CAPLUS
CN L-α-Asparagine, N-[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-N-[(3S)-1-(2-amino-2-oxoethyl)hexahydro-1H-azepin-3-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:106085 CAPLUS
DOCUMENT NUMBER: 128:176149
TITLE: Molecular model for VLA-4 inhibitors, and inhibitor identification
INVENTOR(S): Singh, Juswinder; Zheng, Zhongli; Sprague, Peter; Van Vlijmen, Herman W. T.; Castro, Alfredo C.; Adams, Steven P.
PATENT ASSIGNEE(S): Biogen, Inc., USA; Singh, Juswinder; Zheng, Zhongli; Sprague, Peter; Van Vlijmen, Herman W. T.; Castro,

Alfredo C.; Adams, Steven P.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804913	A1	19980205	WO 1997-US13008	19970724
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2261974	A1	19980205	CA 1997-2261974	19970724
AU 9737385	A	19980220	AU 1997-37385	19970724
EP 914605	A1	19990512	EP 1997-934288	19970724
EP 914605	B1	20070530		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, LT, LV, RO, SI				
CN 1230110	A	19990929	CN 1997-197953	19970724
HU 9903142	A2	20000128	HU 1999-3142	19970724
HU 9903142	A3	20000628		
CN 1478472	A	20040303	CN 2003-2003146679	19970724
SG 124234	A1	20060830	SG 2001-382	19970724
AT 339196	T	20061015	AT 1997-934289	19970724
ES 2271971	T3	20070416	ES 1997-934289	19970724
CZ 298080	B6	20070613	CZ 1999-232	19970724
AT 363658	T	20070615	AT 1997-934288	19970724
CZ 298089	B6	20070620	CZ 2003-1362	19970724
ES 2285735	T3	20071116	ES 1997-934288	19970724
KR 2000029538	A	20000525	KR 1999-700595	19990125
US 6552216	B1	20030422	US 1999-236784	19990125
BG 64470	B1	20050430	BG 1999-103193	19990222
BG 108806	A	20050430	BG 1999-108806	19990222
BG 64902	B1	20060831		
AU 759063	B2	20030403	AU 2001-91330	20011114

PRIORITY APPLN. INFO.:

US 1996-22890P	P	19960725
US 1996-32786P	P	19961206
US 1997-57002P	P	19970630
AU 1997-37386	A3	19970724
WO 1997-US13008	W	19970724

OTHER SOURCE(S): MARPAT 128:176149

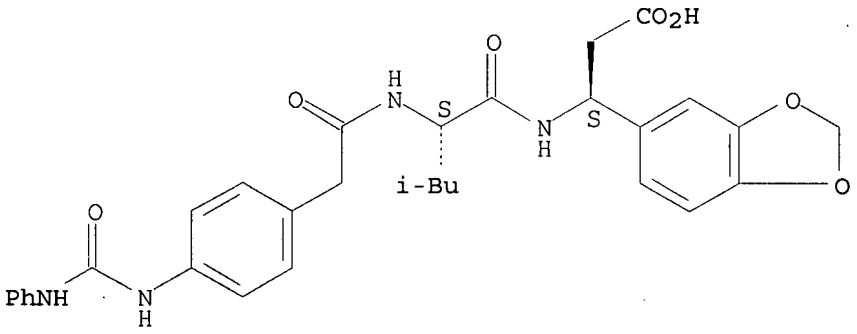
AB Pharmacophore models of VLA-4 inhibitors are disclosed, as are methods of identifying novel inhibitors and novel inhibitors identified by these methods.

IT 181520-66-1 181523-34-2 187735-94-0
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. model for VLA-4 inhibitors, and inhibitor identification)

RN 181520-66-1 CAPLUS

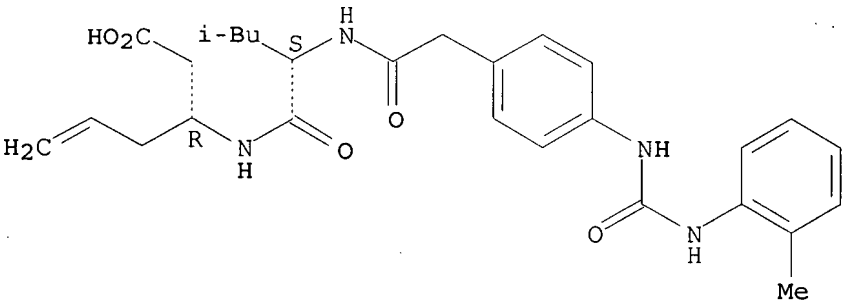
CN 1,3-Benzodioxole-5-propanoic acid, β-[[(2S)-4-methyl-1-oxo-2-[[[4-[[(phenylamino)carbonyl]amino]phenyl]acetyl]amino]pentyl]amino]-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



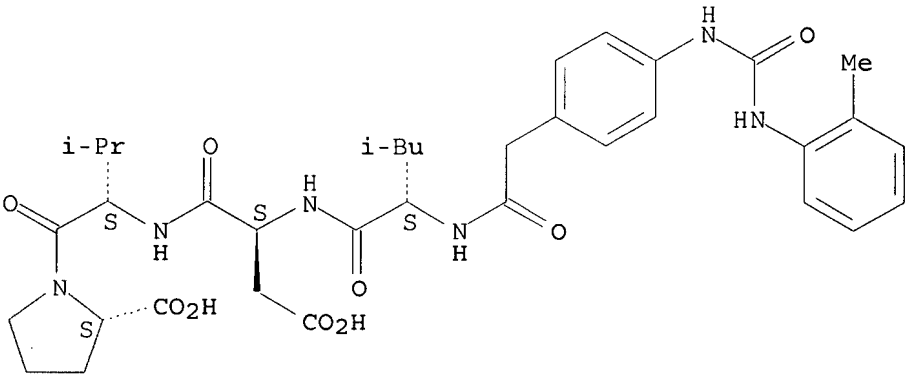
RN 181523-34-2 CAPLUS
CN 5-Hexenoic acid, 3-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187735-94-0 CAPLUS
CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

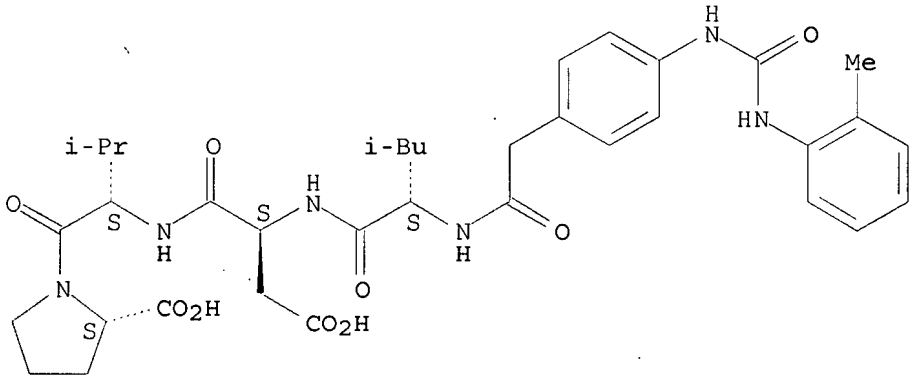
L7 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:395127 CAPLUS
DOCUMENT NUMBER: 127:103716

TITLE: Potent antagonists of the leukocyte integrin alpha-4 beta-1 (VLA-4)
AUTHOR(S): Adams, Steve
CORPORATE SOURCE: Biogen, USA
SOURCE: Drug Discovery Technology: Interdisciplinary Approaches to Accelerate Drug Development, [IBC Conference, "Drug Discovery Technology: Interdisciplinary Approaches to Accelerate Drug Development"], Boston, Aug. 19-22, 1996 (1997), Meeting Date 1996, 5.2.1-5.2.18. Editor(s): Hori, Wendy. International Business Communications: Southborough, Mass.
CODEN: 64OVAX
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with no cited refs. The role of leukocyte α-4β-1 integrin (VLA-4) in the pathogenicity of inflammatory diseases are discussed. Using a classical peptide mimetic approach, very potent sub-nanomolar inhibitors of VLA-4 have been developed. Candidate VLA-4 inhibitors (e.g., BIO-1211) are highly selective, and some are equipotent against α-4β-7. The different classes of compds. that have been identified are exquisitely potent in the DTH model and are also very potent in a pathophysiol. model of airway hyper-responsiveness. BIO-1211 is currently in late stage of preclin. development.

IT 187735-94-0, BIO 1211
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent antagonists of the leukocyte α4β1-integrin (VLA-4))
RN 187735-94-0 CAPLUS
CN L-Proline, N-[2-[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl- (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:207658 CAPLUS
DOCUMENT NUMBER: 126:199840
TITLE: Preparation of peptide derivatives as cell adhesion inhibitors
INVENTOR(S): Lin, Ko-Chung; Adams, Steven P.; Castro, Alfredo C.; Zimmerman, Craig N.; Cuervo, Julio Hernan; Lee, Wen-Cherng; Hammond, Charles E.; Carter, Mary Beth; Almquist, Ronald G.; Ensinger, Carol Lee
PATENT ASSIGNEE(S): Biogen, Inc., USA; Lin, Ko-Chung; Adams, Steven, P.; Castro, Alfredo, C.; Zimmerman, Craig, N.; Cuervo,

Julio, Hernan; Lee, Wen-Cherng; Hammond, Charles, E.; Carter, Mary, Beth; et al.

SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

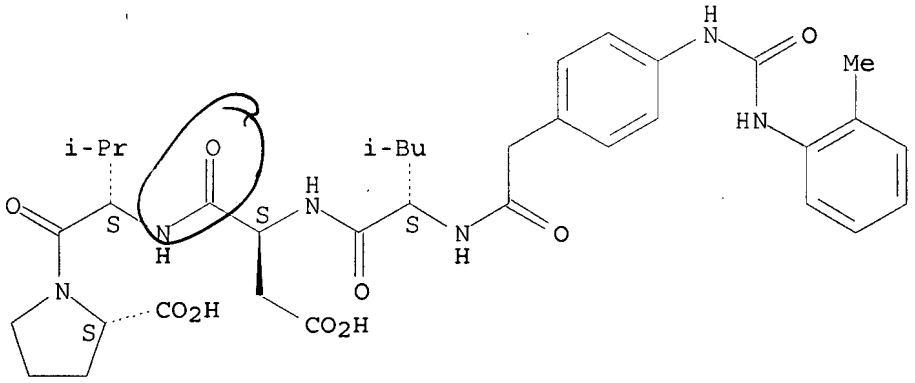
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703094	A1	19970130	WO 1996-US11570	19960711
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 6248713	B1	20010619	US 1995-498237	19950711
CA 2226868	A1	19970130	CA 1996-2226868	19960711
AU 9664894	A	19970210	AU 1996-64894	19960711
AU 716276	B2	20000224		
EP 842196	A1	19980520	EP 1996-924444	19960711
EP 842196	B1	20071121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1193325	A	19980916	CN 1996-196380	19960711
HU 9802202	A2	19990128	HU 1998-2202	19960711
BR 9609782	A	19990309	BR 1996-9782	19960711
JP 11511124	T	19990928	JP 1996-505989	19960711
NZ 312950	A	20000128	NZ 1996-312950	19960711
EE 3694	B1	20020415	EE 1997-362	19960711
EE 200200384	A	20021015	EE 2002-384	19960711
PL 188446	B1	20050228	PL 1996-324491	19960711
IL 122783	A	20050831	IL 1996-122783	19960711
RO 121032	B1	20061130	RO 1998-33	19960711
TW 570927	B	20040111	TW 1996-85108493	19960712
FI 9800033	A	19980305	FI 1998-33	19980109
NO 9800097	A	19980311	NO 1998-97	19980109
BG 63876	B1	20030430	BG 1998-102241	19980210
US 6239108	B1	20010529	US 1998-983391	19980810
US 6596687	B1	20030722	US 2000-482296	20000113
AU 758886	B2	20030403	AU 2000-36445	20000525
US 6875743	B1	20050405	US 2000-724139	20001128

PRIORITY APPLN. INFO.:

US 1995-498237	A	19950711
AU 1996-64894	A3	19960711
WO 1996-US11570	W	19960711
US 1998-983391	A1	19980810

OTHER SOURCE(S): MARPAT 126:199840

AB The present invention relates to novel peptide derivs. that are useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. This invention also relates to pharmaceutical formulations comprising these compds. and methods of using them for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. The compds. and pharmaceutical composition of this invention can be used as therapeutic or prophylactic agents. They are particularly well-suited for treatment of many inflammatory and autoimmune diseases. Thus, coupling of 4-(2-MeC6H4NHCONH)C6H4CH2CO2H (preparation given) with protected peptide H-Leu-Asp(OCH2Ph)-Val-OCH2Ph (preparation given), followed by catalytic hydrogenolysis, gave cell adhesion inhibitor peptide 4-(2-MeC6H4NHCONH)C6H4CH2CO-Leu-Asp-Val-OH (I). All 408 prepared peptide derivs., including I, inhibited VLA4-dependent adhesion to a bovine serum albumin conjugate with H-Cys-Tyr-Asp-Glu-Leu-Pro-Gln-Leu-Val-Thr-Leu-Pro-



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CRN 77-86-1
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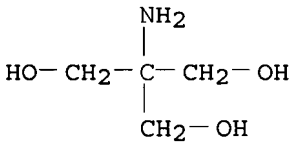
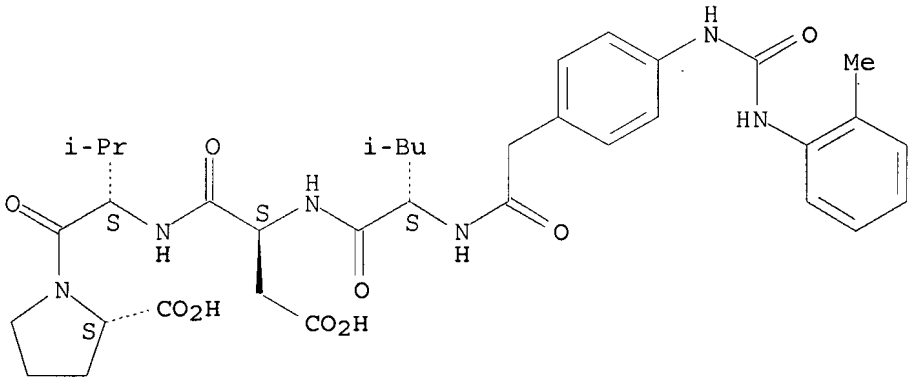


RN 187737-53-7 CAPLUS
CN L-Proline, N-[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-L-leucyl-L-α-aspartyl-L-valyl-, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 Na

Inventors

L7 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:593835 CAPLUS
DOCUMENT NUMBER: 125:248489
TITLE: Preparation of dipeptide derivatives as cell adhesion inhibitors

10/679,478

INVENTOR(S): Adams, Steven P.; Lin, Ko-Chung; Lee, Wen-Cherng; Castro, Alfredo C.; Zimmerman, Craig N.; Hammond, Charles E.; Liao, Yu-Sheng; Cuervo, Julio Hernan; Singh, Juswinder

PATENT ASSIGNEE(S): Biogen, Inc., USA

SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622966	A1	19960801	WO 1996-US1349	19960118
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
US 6306840	B1	20011023	US 1995-376372	19950123
CA 2211181	A1	19960801	CA 1996-2211181	19960118
AU 9649115	A	19960814	AU 1996-49115	19960118
AU 718926	B2	20000504		
EP 805796	A1	19971112	EP 1996-905316	19960118
EP 805796	B1	20021211		
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BR 9606778	A	19980106	BR 1996-6778	19960118
CN 1177343	A	19980325	CN 1996-192270	19960118
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ES 2183937	T3	20030401	ES 1996-905316	19960118
CZ 291556	B6	20030416	CZ 1997-2340	19960118
PT 805796	T	20030430	PT 1996-905316	19960118
EE 4111	B1	20030815	EE 1997-172	19960118
SK 283724	B6	20031202	SK 1997-987	19960118
PL 187313	B1	20040630	PL 1996-321848	19960118
RO 119885	B1	20050530	RO 1997-1369	19960118
TW 500714	B	20020901	TW 1996-85100690	19960122
IL 116846	A	20021110	IL 1996-116846	19960122
NO 9703384	A	19970919	NO 1997-3384	19970722
NO 320914	B1	20060213		
FI 9703087	A	19970922	FI 1997-3087	19970722
BG 63383	B1	20011231	BG 1997-101841	19970821
US 6376538	B1	20020423	US 1997-875321	19970919
HK 1005241	A1	20030822	HK 1998-104006	19980508
AU 766538	B2	20031016	AU 2000-62432	20001002
US 2003083267	A1	20030501	US 2001-935461	20010822
US 6624152	B2	20030923		
US 2003018016	A1	20030123	US 2001-2341	20011023
US 6630512	B2	20031007		
US 7001921	B1	20060221	US 2003-625626	20030724
US 2006166866	A1	20060727	US 2003-679478	20031007

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AU 1996-49115	A3	19960118
EP 1996-905316	A3	19960118

WO 1996-US1349 W 19960118
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OTHER SOURCE(S): MARPAT 125:248489

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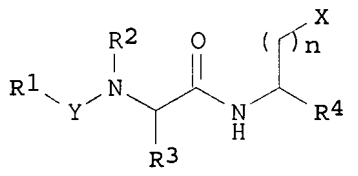

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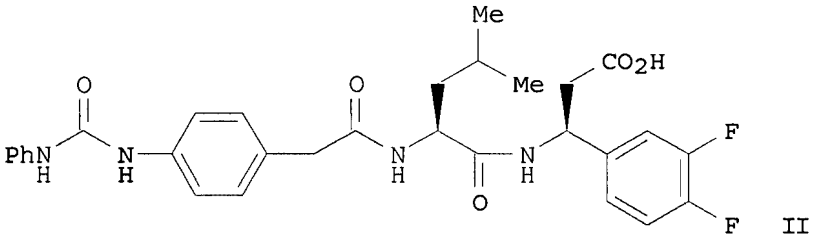

II

AB Novel dipeptide analogs I [X = CO2H, PO3H-, SO2R5, SO3H, OPO3H-, CO2R4, CONR42; Y = CO, SO2, PO2; n = 0-2; R1 = optionally substituted alkyl, alkenyl, alkynyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl, alkoxy, alkenyloxy, aralkoxy, alkylamino, alkenylamino, alkynylamino, aryloxy, arylamino, N-alkylurea-substituted alkyl, heterocyclyl; R2 = H, aryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl-substituted alkyl; R2NCR3 = heterocyclic ring; R3 = natural, unnatural, modified, or substituted amino acid side chain; R4 = optionally substituted aryl, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl-substituted alkyl, H, heterocyclyl, heterocyclylcarbonyl, aminocarbonyl, amido, alkylaminocarbonyl, arylaminocarbonyl, acylaminocarbonyl, acyl; R5 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl] are prepared as compds. useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. This invention also relates to pharmaceutical formulations comprising these compds. and methods of using them for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. The compds. and pharmaceutical compns. of this invention can be used as therapeutic or prophylactic agents. They are particularly well-suited for treatment of many inflammatory and autoimmune diseases. Thus, β-amino acid-containing dipeptide II, prepared by standard methods, displayed an IC50 of <50 nM in a cell adhesion inhibition assay.

IT 181520-66-1P 181520-79-6P 181520-82-1P
181520-85-4P 181520-90-1P 181520-95-6P
181521-01-7P 181521-05-1P 181521-13-1P
181521-26-6P 181521-28-8P 181521-42-6P
181521-45-9P 181522-35-0P 181522-44-1P
181522-47-4P 181522-51-0P 181522-53-2P
181522-61-2P 181522-65-6P 181522-70-3P
181522-71-4P 181522-73-6P 181522-78-1P
181522-79-2P 181522-81-6P 181522-82-7P
181522-83-8P 181522-84-9P 181522-85-0P
181522-86-1P 181522-94-1P 181522-95-2P
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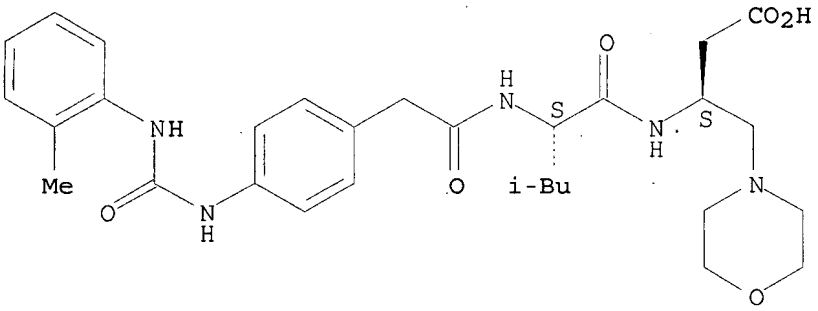
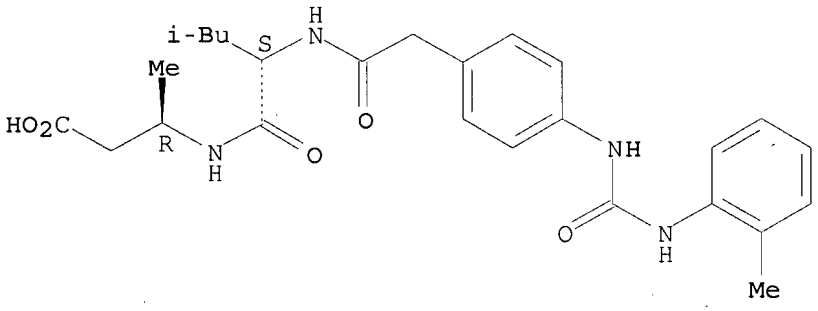


IT 181525-87-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of β-amino acid dipeptide derivs. as cell adhesion inhibitors)
RN 181525-87-1 CAPLUS
CN Butanoic acid, 3-[[(2S)-4-methyl-2-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L6 134 S L4 FULL

FILE 'CAPLUS' ENTERED AT 14:15:51 ON 29 NOV 2007
L7 26 S L6

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.